White Paper

# Liver Total Approach

Courtesy of
Prof. Clevert, Prof. Filice and Dr. Maiocchi

esaote

## Introduction

Initial screening for a liver condition usually starts with an ultrasound scan and blood tests and may be followed by other imaging tests, such as CT or MRI, to obtain further information. Ultrasound is particularly suitable for differentiating solid masses from liquid ones. In addition, an ultrasound examination can evaluate diffuse liver diseases, like fatty liver or hepatitis. Nowadays, the extended connectivity and the multimodality approach open new horizons in radiology imaging, where ultrasound devices may play a central role in Cross-Modality Imaging.

## Background

The first real-time sonography device, the so-called “fast B-scan”, was introduced in 1965. Sonography has been an essential part of daily clinical diagnostics for more than 50 years and is guided by the most modern technological developments. Over the last 20 years, many technological advances, such as advanced signal processing and new transducer generation, have been reached to push the limitations of ultrasound techniques to provide excellent image quality for screening and monitoring. Furthermore, intensive research and developments led to the creation and integration of new technologies that can be grouped into four major diagnostic tools:

### 1) Elastosonography and 2D Shear-Wave techniques

2D Shear-Wave elastosonography enables a stiffness map and quantitatively assesses the tissue stiffness.

### 2) Attenuation imaging

Attenuation imaging enables the visualisation and quantification of the attenuation along the liver depth to assess hepatic steatosis.

### 3) Contrast-Enhanced Ultrasound (CEUS)

The ultrasound contrast agent, CEUS makes it possible to detect organ perfusion and additionally characterise liver lesions.

### 4) Fusion imaging

Fusion imaging technology combines an existing CT or MRI dataset with a real-time ultrasound examination.

Following a description of the main technologies used in screening and monitoring, these new techniques, briefly outlined here, will be reported in detail below.

## Ultrasound liver screening and monitoring

The echo structure and vascularisation are the two main elements of liver screening. Because of wide interpatient variability (due to the presence of fat, gas, or other factors), the quality of liver visualisation and lesion detection may be affected. Esaote has developed specific technologies to overcome the limitations of the ultrasound technique and provide excellent image quality even in challenging patients and conditions.

### XCrystal probe technology

Associated with the new generation of signal post-processing, XCrystal technology enables details sharpness even in very deep areas to achieve homogenous and resolutive images **(Fig. 1)**. Furthermore besides traditional shape of convex transducers, Esaote offers a Zero-degree biopsy probe to facilitate the interventional procedure **(Fig. 2)**.

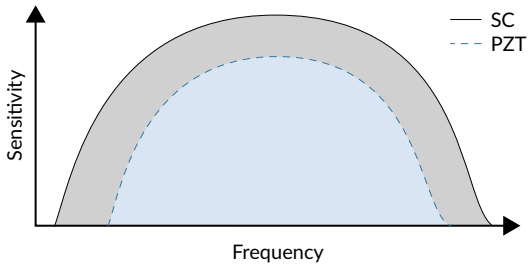


*Fig. 1: Sensitivity graph comparing the usage of a single crystal array versus a PZT technology array*

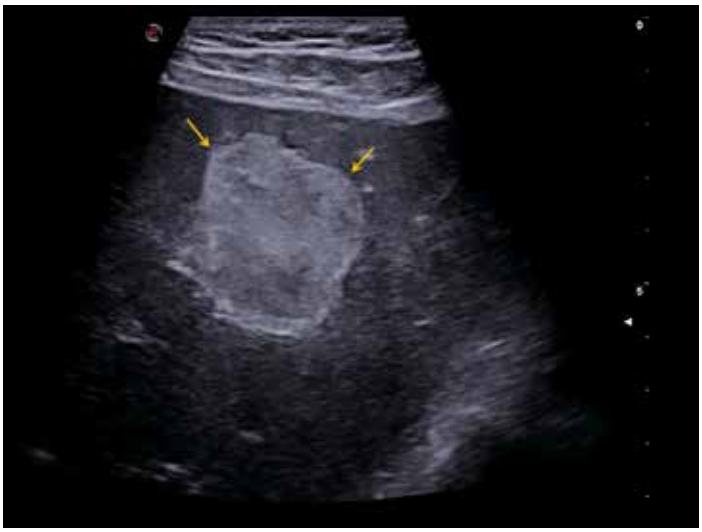

*Fig. 2: 36 year-old male patient with a large, hyperechoic lesion (yellow arrows) in a non-cirrhotic liver in B-mode ultrasound imaging*

### microV

Esaote has developed an adaptive algorithm that effectively separates flow signals from overlaying tissue motion artefacts and background noise. microV is the latest technology by Esaote, with a high degree of sensitivity even for very small vessels and slow flows, which enables hemodynamic evaluation with high sensitivity and high spatial resolution **(Fig. 3)**.

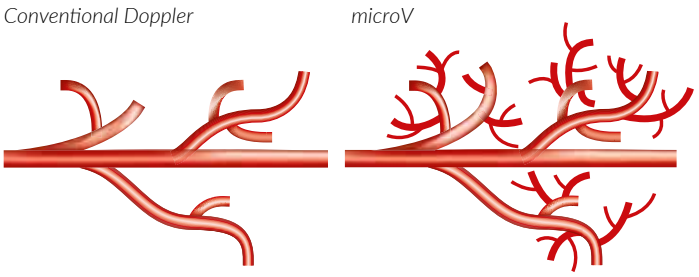


*Fig. 3: Image representing sensitivity in terms of vascularisation visualisation between Power Doppler Technique and microV technology.*

microV can distinguish between signals coming from flows and other sources with very low flow signal preservation compared to conventional Doppler techniques **(Fig. 4)**.

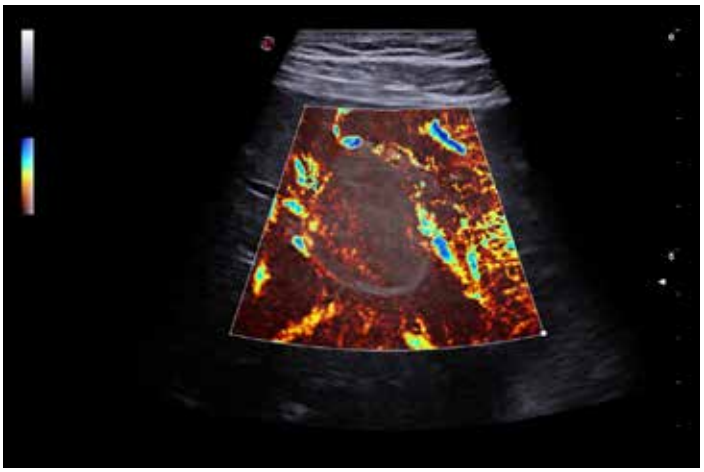

*Fig. 4: The hyperechoic lesion does not display any increase in vascularisation with microV technology*

"Staging liver fibrosis and portal hypertension are important for monitoring, prognosis and treatment. In the meantime, the ultrasound attenuation imaging technique may become a promising method of choice for the assessment of liver steatosis."

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## Stiffness and Attenuation Assessment

### Background

Chronic liver disease is a worldwide problem with causes ranging from viral infection and NAFLD (nonalcoholic fatty liver disease) to ALD (alcoholic liver disease), cholestatic liver disease and AIH (autoimmune hepatitis), all resulting in an abnormal increase in collagen deposition and other components of the extracellular matrix in the liver. This leads to liver cirrhosis, with ensuing portal hypertension, impaired liver function, decompensated liver cirrhosis (ascites, encephalopathy, variceal haemorrhage, jaundice) and hepatocellular carcinoma.

Staging liver fibrosis and portal hypertension are important for monitoring, prognosis and treatment.

Liver biopsy and catheter-directed measurement of the hepatic venous pressure gradient (HVPG) remain the benchmark diagnostic methods, but they are invasive, with possible morbidity and may require hospitalisation. Liver biopsy (LB) is the gold standard for assessing liver fibrosis, but known limitations are small sample size (1/5000 x the whole liver tissue) with possible sampling error and wide inter-observer variability. As an invasive procedure, it is also not readily accepted by many patients. Moreover, HVPG measurement is available in expert centres only.

Non-invasive methods of fibrosis evaluation have been developed to address these problems, and elastographic techniques – which provide a surrogate biomarker of liver fibrosis – are currently considered viable alternatives to liver biopsy in several clinical scenarios.

According to EFSUMB and WFUMB guidelines[1,2] the US elastography can be divided into strain elastography (SE) and shear-wave elastography (SWE). The latter includes vibration-controlled transient elastography (TE, FibroScan, Echosens, Paris, France), performed with a dedicated device, and acoustic radiation force impulse (ARFI) techniques, performed with ultrasound systems. The ARFI techniques are point shear-wave elastography (SWE) and 2D-SWE.

The 2D-SWE ultrasound technique has several advantages, as it is:

- non-invasive
- complementary to a B-Mode liver evaluation
- less expensive than MRI elastography
- more available than MRI elastography
- an easy and repeatable technique

Due to the overlap between stiffness values, guidelines do not suggest the use of SWE to differentiate benign and malignant focal liver lesions, but they recommend SWE techniques:

- to rule out compensated advanced chronic liver disease (cACLD) when in agreement with the clinical and laboratory data and values are within the normal range
- to rule out cirrhosis
- to evaluate, as a first-line assessment, the severity of liver fibrosis even if they are much less reliable in differentiating intermediate stages of fibrosis[3].

For all equipment, a SWE measurement within the normal range, in a subject without other clinical or laboratory evidence of liver disease, may exclude significant liver fibrosis with a high degree of certainty. For both VCTE and ARFI-based techniques, there is consensus that values ≤5 kPa (1.3 m/s) are highly likely to be normal.

In 2020, an update to the Society of Radiologists' Ultrasound Liver Elastography Consensus Statement proposed a neutral "rule of four" (5, 9, 13, 17 kPa) for ARFI techniques for viral etiologies and NAFLD[4].

This rule proposes different cut-offs for the interpretation of liver stiffness:

- 5 kPa (1.3 m/sec) or lower: highly likely to be normal
- lower than 9 kPa (1.7 m/sec): in the absence of other known clinical signs, rules out cACLD
- between 9 kPa (1.7 m/sec) and 13 kPa (2.1 m/sec): suggestive of cACLD but may need further tests for confirmation
- higher than 13 kPa (2.1 m/sec): highly suggestive of cACLD
- higher than 17 kPa (2.4 m/sec), probability of CSPH but additional patient testing may be required.

Even in case of NAFLD, the cut-off values for cACLD may be lower and a follow-up or additional testing is recommended in patients with values between 7 and 9 kPa.

Hepatic steatosis is the main manifestation of non-alcoholic fatty liver disease (NAFLD), the prevalence of which reaches 16-30% within the general population, both adults and children. It is higher in cases of severe obesity and in patients with metabolic syndrome and type-2 diabetes mellitus. The main characteristic of NAFLD is the high quantity of fat stored in liver cells due to the accumulation of triglycerides and fats within the hepatocytes, reflecting impairment of normal processes of synthesis and elimination of fat.

Despite liver biopsy and MRI proton density fat fraction (MRI-PDFF)[5-9] being methods of choice for evaluating the fat infiltration in the liver, ultrasound signal rate of attenuation along the depth appears to be a strongly positively parameter correlated to liver fat content[10].

The attenuation rate is a quantitative measure, and therefore less operator-dependent, can be interpreted using clinical and laboratory data, enabling the evaluation of steatosis, particularly for patient follow-up.

Attenuation measurement can be provided as a single global measure over a Region of Interest (ROI) or as a colour-coded image overlapped with the B-Mode image, encoding the local attenuation value for each pixel.

Ultrasound attenuation imaging technique may become a promising method of choice for the assessment of liver steatosis for several advantages, such as the fact that it is non-invasive, complementary to a B-Mode liver evaluation, less expensive and more available than MRI examination, and a repeatable technique.

## Esaote QElaXto 2D technology

QElaXto 2D is a Shear-Wave Elastosonography (SWE) technique from Esaote that alternates multiple perturbations and reading phases, making it possible to detect stiffness in a small tissue sample. The system creates multiple shocks close to the sample box, that induce shear-waves. It then tracks the radiofrequency (RF) signal of the tissue displacement on different strips of the sample inside the box and measures the shear-wave velocity for each strip. Secondly, the velocity is associated with a colour map, then QElaXto 2D encodes each strip with colour pixels, to produce a multi-coloured representation of the stiffness in the sample **(Fig. 5)**. The operator has the option to change the scale of the stiffness representation, which can be reported in either m/s or kPa[11-12].

To help clinicians obtain reliable measurements, QElaXto 2D offers additional tools, namely a dispersion map and rejection parameter. The dispersion map is the computation of the standard deviation of the value of each pixel in comparison with the surrounding ones.

- Green indicates that the reliability is good
- Orange indicates that the reliability is weak

It can be enabled in addition to stiffness imaging in a dual-mode visualisation.

The rejection parameter indicates to the algorithm the rejection level for the artefacts, vessels, and weak shear-waves. With rejection activated, the algorithm does not include the pixels from the rejected areas in the computation of the values.

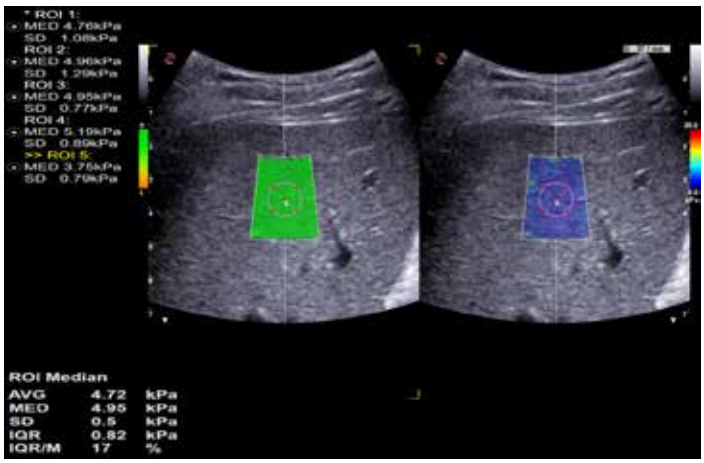



*Fig. 5: 2D-SWE examination in a healthy patient with a median value of 4.72 kPa and IQR/m of 17%. The quality map on the left side of the image is highlighted in green to indicate a high-quality examination*

## Esaote QAI Technology

QAI (Q-Attenuation Imaging) is an ultrasound technique for the visualisation and quantification of the attenuation along the liver depth to understand the information displayed during the fat content assessment from Esaote S.p.A. (Genoa, Italy). QAI is evaluated on the MyLab™9eXP ultrasound platform and provides a quantitative liver attenuation assessment with the probe C 1-8, a single crystal convex transducer. When QAI is active, a dedicated menu is displayed on the touchscreen to facilitate the workflow and acquisitions. The US tissue signal decays exponentially according to penetration depth, with a factor depending on frequency and on attenuation rate, which is characteristic for the specific tissue.

QAI enables a real-time, continuous colour-coded image of the attenuation inside the ROI and offers a dual display mode **(Fig. 6)**. The operator can adjust the transparency of the colour-coded image of the attenuation visualisation.

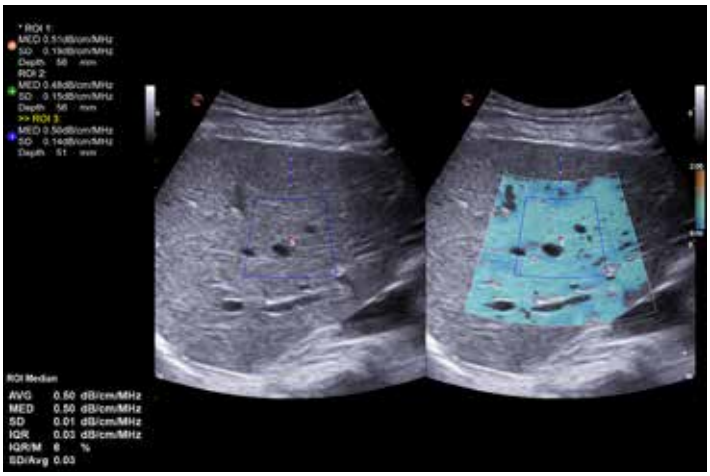



*Fig. 6: QAI technology – QAI acquisition on a patient with dual-mode visualisation. The automatic rejection parameter can cope with speckle, electronic noise, and local variations in echogenicity, and reject them in the colour-coded representation of the attenuation*

## Esaote QAI and QElaXto 2D measurements

Clinicians must perform five valid measurements inside the sample box to obtain a quantitative assessment, by putting the measurement ROI (region of interest) – which can be a manual trace, a circle, an ellipse, or a vertex – in an area of the liver, free from vessels, bile ducts, and artefacts. Consequently, clinicians can perform a quantitative measurement inside the box, placing the ROI in an area free of vessels, bile ducts, and artefacts.

QElaXto 2D and QAI can provide the following measurements:

- Median (MED) in kPa or m/s for QElaXto 2D and dB/cm/MHz for QAI
- IQR/MED in %

The software also provides additional measurements, such as:

- Average (AVG) in kPa or m/s for QElaXto 2D and dB/cm/MHz for QAI
- Standard Deviation (SD) in kPa or m/s for QElaXto 2D and dB/cm/MHz for QAI
- Interquartile Range (IQR) in kPa or m/s for QElaXto 2D and dB/cm/MHz for QAI

According to the guidelines, three to five valid measurements are adequate in the presence of a quality assessment provided by the manufacturer. The session (ended after five good acquisitions) can be considered reliable when IQR/MED < 30%.

*Fig. 7: Patient position for a 2D-SWE examination – Patient in decubitus position with his right arm above his head and the convex probe on the intercostal access*

## General recommendations for QElaXto 2D[14]

- Measurement of liver stiffness by SWE should be performed through the right intercostal space in a supine position, with the right arm extended, with the patient holding their breath, avoiding deep inspiration beforehand **(Fig. 7)**
- Measurement of liver stiffness by SWE should be performed by experienced operators
- Measurement of liver stiffness by 2D-SWE should be performed at least 10 mm below the liver capsule
- Patients should fast for a minimum of 2-4 hours and rest for a minimum of 10 minutes before undergoing liver stiffness measurement (LSM) with SWE
- The major potential confounding factors (liver inflammation indicated by AST and/or ALT elevation > 5 times the normal limits, obstructive cholestasis, liver congestion, acute hepatitis, and infiltrative liver diseases) should be ruled out before performing LSM with SWE, to avoid an overestimation of liver fibrosis and/or should be considered when interpreting the SWE results
- SWE within the normal range can rule out significant liver fibrosis when the clinical and laboratory background allows
- Adequate B-Mode liver imaging is a prerequisite for 2D-SWE measurements
- For 2D-SWE, a minimum of three to five measurements should be obtained; the final result should be expressed as the median together with the interquartile range. An IQR/M ≤ 30% is the most important reliability criterion
- The results with the lowest variability in 2D-SWE systems may be obtained at a depth of 4–5 cm from the transducers.

## The Society of Radiologists update on ultrasound

As suggested by the latest guidelines, the evaluation of the progression of liver diseases and the staging of liver diseases are the most important factors for evaluating the prognosis, monitoring and treatment indications, given that fibrosis is a dynamic process and patients with a higher stage of liver fibrosis (F3-F4) are at higher risk of clinical complications. Therefore, a consensus panel recently suggested the vendor-independent "rule of four" (5, 9, 13, 17 kPa) for the RF pulse energy techniques **(Table 1)**. The rule of four should be used in hepatopathies of viral etiologies and in patients with NAFLD.

For other etiologies, such as alcoholic hepatitis, primary biliary cirrhosis, Wilson disease, autoimmune hepatitis, sclerosing cholangitis, and drug-induced liver disease, there is as yet insufficient data to give the same indication.

| Liver Stiffness | Recommendations |
|---|---|
| ≤ 5 kPa (1.3 m/sec) | Highly likely to be normal |
| < 9 kPa (1.7 m/sec) | Without other clinical signs, rules out cACLD. In presence of clinical signs, may need a further test for confirmation |
| 9-13 kPa (1.7-2.1 m/sec) | Suggestive of cACLD but needs further test for confirmation **(Fig. 8)** |
| 17 kPa (2.4 m/sec) | Suggestive of CSPH |

*Keys: cACLD = compensated advanced chronic liver disease; CSPH = clinically significant portal hypertension*

*Table 1: Rule of four established for the use of 2D-SWE technique in ultrasound for fibrosis staging*

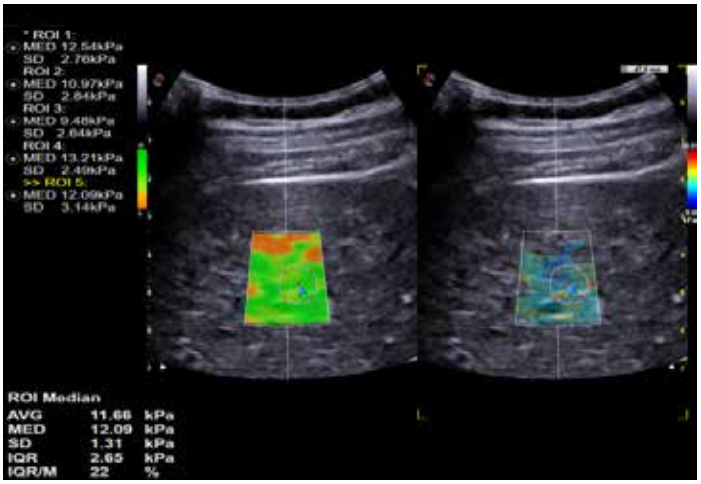



*Fig. 8: 2D-SWE examination performed on a patient with known hepatitis C. A median value of 11.66 kPa and IQR/M of 22% were measured. The quality map confirmed the quality of the examination*

## Cut-off for Esaote systems regarding steatosis and fibrosis

A study is underway in patients with metabolic diseases, in which the Esaote US system measures liver stiffness and attenuation.

Liver fibrosis and steatosis are quantified by liver biopsy and we will provide our cut-off values both for significant fibrosis and steatosis.

The first results showed good intra– and inter-observer reproducibility and suggested cut-offs of 0.61 dB/cm/MHz for mild steatosis (S >1) and 0.72 dB/cm/MHz for significant steatosis (S>2)[13].

"Real technological developments have been integrated with elastosonography techniques and fusion imaging for use during liver ultrasound examinations. Over the past 10 years, ultrasound tools like CEUS, have become invaluable in the follow-up of patients."

Prof. Dirk-André Clevert
Head of Ultrasound Department – Munich University, Germany

## Detection and characterization of liver lesions by contrast agent enhancement

### Background

Liver ultrasound scans are commonly used as first-line imaging for evaluating focal liver lesions. It is important to differentiate benign masses from malignant ones. The liver is the most common site of metastatic lesions. Approximately 25-50% of patients with a primary malignancy have liver metastases at the time of diagnosis[15], while the prevalence of liver lesions in the general population is only about 5%[16].

Determining further therapy (surgical resection versus interventional therapy) depends on the size, number, and location of the liver metastases[17].

Therefore, accurate detection[18,19] and characterisation of hepatic masses are important for determining disease prognosis and making decisions regarding patient management.

Since non-invasive techniques cannot provide a tissue diagnosis, histopathology of core biopsies is the gold standard for the final diagnosis of liver lesions[20].

An enhanced ultrasound examination is often labelled as a contrast-enhanced ultrasound or CEUS examination. Each examination starts with a patient informed consent form. This form should include information about the potential risks and side effects, such as an anaphylactic reaction. The incidence of allergic reactions is reported in the literature as up to 1/10,000 cases. In comparison with iodine-containing contrast agents used in multi-slice computed tomography, the risk is much lower[21,22]. There have been no reports of cardio–, nephro–, thyroid, or hepatotoxicity following ultrasound contrast agent administration; it is, therefore, unnecessary to request or check laboratory values before the examination[20,22,23].

In Europe, SonoVue®* from the Bracco Company (Milan, Italy) is available as an ultrasound contrast agent. This contrast agent contains 1-10 µm in size microbubbles, which include an inert gas known as "sulfur hexafluoride". The bubbles are stabilised by a phospholipid shell. In comparison with the contrast agents for computed tomography and magnetic resonance imaging, which pass into the interstitial space, this ultrasound contrast agent remains in the vascular space. This technique allows us to detect organ perfusion in real-time imaging[21,25-28]. Gas components of the ultrasound contrast agent will be eliminated via the respiratory tract.

### CnTI™ - Esaote Contrast Enhanced Ultrasound Technology

CnTI™ (Contrast Tuned Imaging) is an Esaote advanced technology for Contrast Enhanced Ultrasound (CEUS) imaging. Based on low mechanical index and real-time scanning, CnTI™ represents the best way to use second-generation contrast media (CM) and prevents the microbubbles from being destroyed too quickly.

### Findings and procedure

Due to the high impedance between blood and bubbles, sound waves will be reflected from the surface of the microbubbles. Furthermore, due to the ultrasound frequency, the microbubbles additionally oscillate generating a contrast-specific signal with higher frequency components[27,28].
For a single CEUS examination, 1.0 to 2.4 cc of the ultrasound contrast agent will be intravenously injected as a bolus. Immediately afterwards, 10 cc of 0.9 % saline is administered as a bolus to flush the IV line[16].
Contrast-enhanced ultrasound of the liver has three overlapping vascular phases after the injection of the contrast agent because of the dual blood supply of the liver, i.e., the hepatic artery and portal vein **(Table 2)**.

- The arterial phase provides information on the degree and pattern of the arterial vascular supply of a focal liver lesion.
- The portal venous phase represents the arrival of an ultrasound contrast agent through the portal system, resulting in diffuse and maximal enhancement of the normal liver parenchyma.
- The late phase lasts until the ultrasound contrast agent is cleared from the circulation and depends on the dose, total scanning time, acoustic power output, and sensitivity of the ultrasound system.

| Phase | Start (sec.) | End (sec.) |
|---|---|---|
| Arterial | 10 – 20 | 30 – 45 |
| Portal venous | 30 – 45 | 120 |
| Late | >120 | bubble disappearance (approx. 4 – 8 min) |

*Table 2: Vascular phases in CEUS of the liver (visualization of post-injection time)[29]*

The potential applications of CEUS imaging include all liver lesions. The lesions can be divided into benign **(Table 3)** and malignant liver lesions **(Table 4)**. Additionally, the liver tissue perfusion and liver vessels can be monitored. In addition to primary diagnostics and intervention, CEUS imaging can be used in the operating room or the intensive care unit.

*SonoVue® is a registered trademark of Bracco Imaging S.p.A.

| Tumor | Arterial phase (10-30 s) | Portal venous phase (10-30 s) | Late phase (10-30 s) |
|---|---|---|---|
| Hemangioma **Fig. 9, 10, 11** | Peripheral nodular enhancement | Partial/complete centripetal fill-in | Incomplete or complete enhancement |
| Focal nodular hyperplasia **Fig. 12, 13, 14** | Hyper-enhancement from the center, complete, early | Hyper-enhancement | Iso-/hyper-enhancing |
| Hepatocellular adenoma | Hyper-enhancement complete | Iso-enhancement | Iso-enhancement |
| Focal fatty infiltration | Iso-enhancement | Iso-enhancement | Iso-enhancement |
| Focal fatty sparing | Iso-enhancement | Iso-enhancement | Iso-enhancement |
| Abscess | Peripheral nodular enhancement, no central enhancement | Hyper/Iso-enhancement rim, no central enhancement | Hypo-enhancing rim, no central enhancement |
| Simple cyst | Non-enhancing | Non-enhancing | Non-enhancing |

*Table 3: Typical enhancement patterns of benign focal liver lesions[29].*

| Tumor | Arterial phase (10-30 s) | Portal venous phase (10-30 s) | Late phase (10-30 s) |
|---|---|---|---|
| Metastasis **Fig. 15, 16, 17** | Rim enhancement | Hypo-enhancement | Hypo-/non-enhancement |
| HCC (Hepato carcinoma) | Hyper-enhancement from the center, complete, early | Iso-enhancement | Hypo-/non-enhancement |
| CCC (Cholangio-carcinoma) | Rim-like hyper enhancement | Hypo-enhancement | Hypo-/non-enhancement |

*Table 4: Typical enhancement patterns of malignant focal liver lesions[29].*

Conventional ultrasound is the most frequently used modality for the primary imaging of abdominal organs, including the liver, but is less sensitive in the detection of focal liver lesions than contrast-enhanced-CT (CECT) and contrast-enhanced-MRI (CEMRI).

Several studies[30-34] have reported that CEUS has a considerably higher sensitivity of up to 80%-90% in detecting liver metastases, comparable to CECT[34] and CEMRI[29,31].

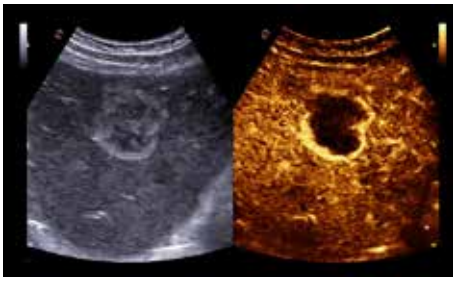


*Fig. 9: Peri-nodule enhancement in arterial phase*

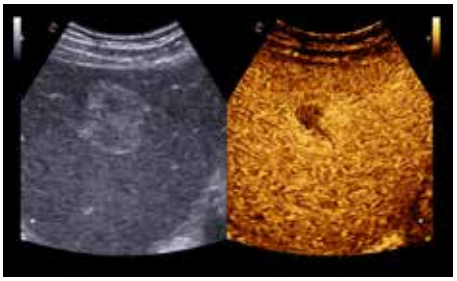


*Fig. 10: Peri-nodule enhancement with nearly complete filling in the portal venous phase*

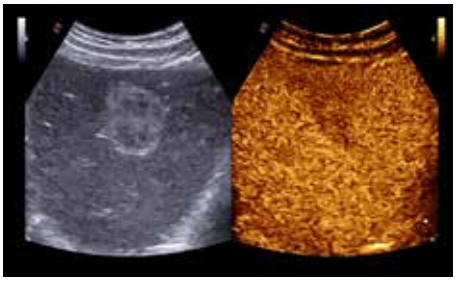


*Fig. 11: Complete filling of the lesion in the late phase; final diagnosis: hemangioma*

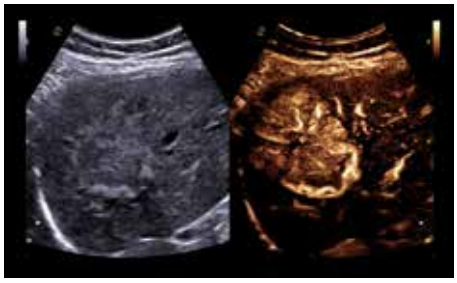


*Fig. 12: Strong early enhancement of the lesion in the arterial phase*

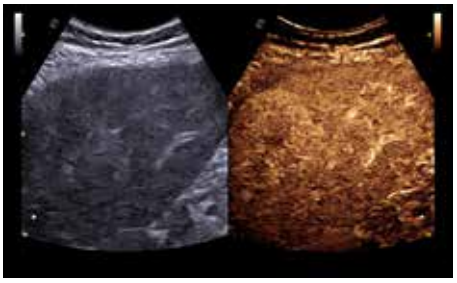


*Fig. 13: Hyper-enhancement of the lesion in the portal venous phase with central scar*

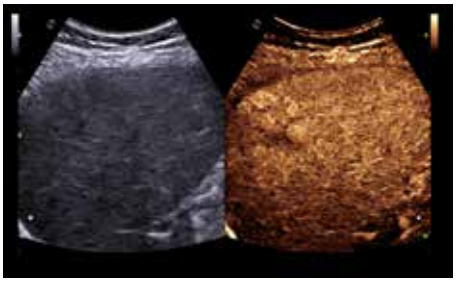


*Fig. 14: Hyper-enhancement in the late phase with central scar; final diagnosis: FNH*

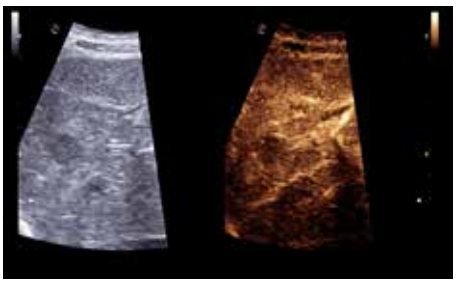


*Fig. 15: Hypo-enhancement in the arterial phase*

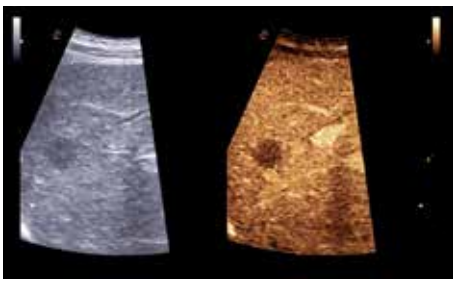


*Fig. 16: Washout in the portal venous phase*

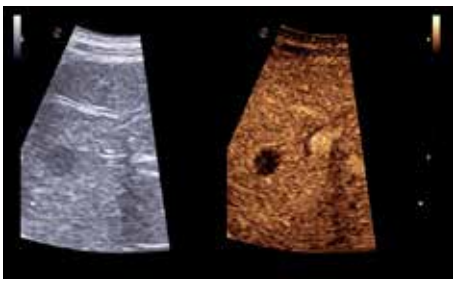


*Fig. 17: Complete washout in the late phase; final diagnosis: liver metastasis*

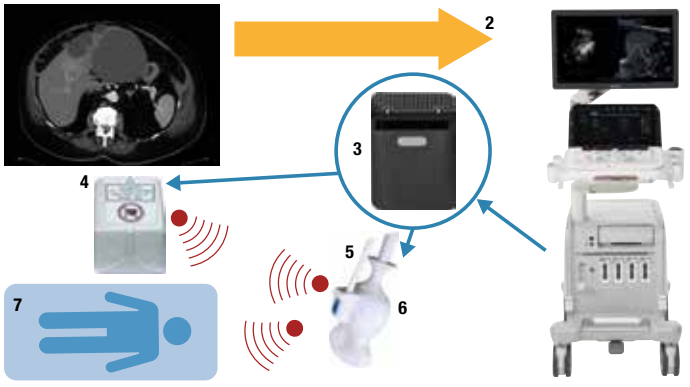
# Fusion imaging with Virtual Navigator

## Background

By providing an additional image from the reference series, fusion imaging enables real-time correlation of anatomy between several imaging modalities, thus making it possible to display continuously reformatted plans from the reference series matching the ultrasound sections. A second modality can be any CT, MR, US, or PET series. It has been possible to fuse existing CT or MRI data on Esaote ultrasound devices since 2004[47-48]. The technology consists of a real-time ultrasound scanner equipped with an electromagnetic tracking device for localising ultrasound transducers and providing their position and orientation in space during a standard liver ultrasound scan. The information from the tracking de- vice and the 3D dataset from the second modality is combined to compute a reformatted slice image that is spatially consistent with the real-time ultrasound image displayed.[50] This advanced ultrasound technique can be useful for complicated liver diseases, especially in the following cases[44,45]:

- Lesions better identified with CT, MRI, or PET or not visible on the US
- Lesions are only seen during arterial phase enhancement
- Follow-up of focal lesion after ablation or resection
- New lesions after previous surgery or ablation
- Lesions are hidden during treatment (the US gassed out)
- Composite ablations requiring multiple needle insertions
- Complex geometries or difficult treatment plans to identify a safe pathway to the target, such as a difficult US "window", or complex insertion angle.

Fusion imaging can also be helpful in young patients and patients with contraindications for CT scans or unclear CT findings, reducing the exposure to radiation as well as to nephrotoxic contrast agents[52-54].




1 *Second Modality Series (CT-scan/MRI)*
2 *Esaote Ultrasound Scanner*
3 *Cable connector on the US scanner*
4 *Electromagnetic Tracking Device (Transmitter)*
5 *Electromagnetic Tracking Antenna (Receiver)*
6 *Ultrasound Probe*
7 *Patient*

*Fig. 18: Tracking solution on Esaote ultrasound system*

## Materials

Virtual Navigator is an Esaote fusion imaging technology. The hardware of the ultrasound system needs an additional magnetic field generator and a position sensor, known as the antenna, for the ultrasound transducer to perform image fusion. The antenna makes it possible to detect the position of the transducer in a three-dimensional field created by the electromagnetic transmitter. Then the software Virtual Navigator enables the co-registration of the datasets from a DICOM[49-50] (digital imaging and communication in medicine) second modality and the real-time ultrasound **(Fig. 18)**.

## Fusion imaging Procedure

The procedure is split into three steps:

### 1. Preparation phase

The operator imports, into the ultrasound device, one or more DICOM second modalities, such as MRI, CT, and PET, directly from the PACS or from an external support, such as a CD or USB stick. Inside the VNav environment, if there is more than one second modality, the operator can use the automatic alignment function to align the series **(Fig. 19)**. Thereafter, the physician identifies the target and fixes it inside the reference volume by selecting "Ball target" or "Auto-contour" on the touchscreen of the VNav menu.

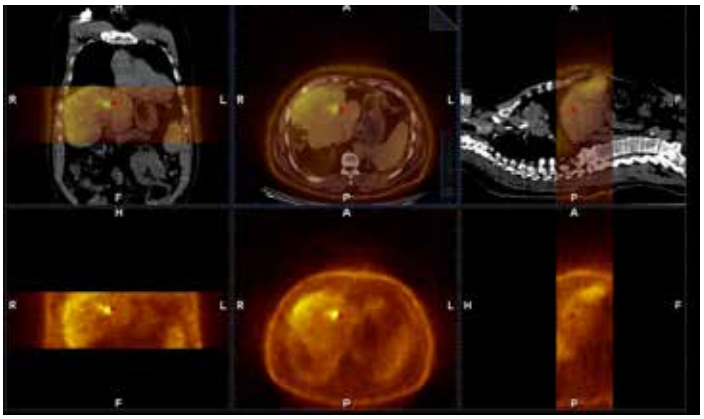


*Fig. 19: Preparation of a fusion imaging procedure with automatic alignment of different DICOM modality datasets and target set*

### 2. Ultrasound/2nd modality dataset co-registration

Once the preparation phase has been completed, the system is ready to start the fusion procedure between MRI or CT and real-time US data. The easiest way is to perform single-plane registration selecting the same plane in axial view both on the US scan and MRI/CT dataset. After confirmation that the system has registered the two modalities, the system will compute a reformatted slice image of the 3D dataset according to the movements of the US transducer. It is recommended to confirm the registration in the same patient of the acquisition using the second modality to increase the accuracy of the alignment. Therefore, some adjustments can be performed to optimise the co-registration closer to the target area. VNav offers different possibilities:

- One-point alignment consisting of a real-time selection of the same point on the US scan and the MRI/CT volume dataset.
- Fine-tuning consists of a real-time selection of the same plan on the US scan and MRI/CT dataset.
- Internal marker alignment using a trigonometry plan in both modalities by selecting at least 3 points.

Usually, the same anatomical landmarks are selected on the US and second modality datasets to perform the alignment adjustment, such as vessels, trying to pick a target where the hepatic vascular pattern presented a bifurcation.

### 3. Navigation phase and interventional procedure

The system is ready to navigate through the two modalities. If more than one-second modality dataset has been uploaded, the operator can switch between them at any time as the reference modality. VNav also offers the possibility to enable a layout with three modalities together. The clinician can proceed to the biopsy or the treatment procedure guided by the second modality **(Fig. 20)** to reach the lesion more confidently.

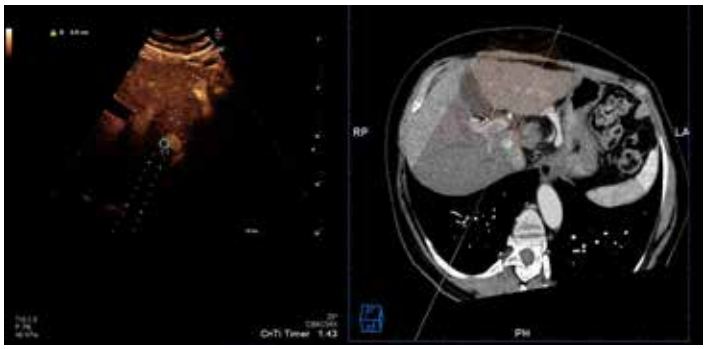


*Fig. 20: Navigation phase enabling the biopsy channel/line on both modalities for performing the interventional procedure*

## Advanced features

VNav technologies offer several advanced tools to facilitate the fusion procedure.

### 1. Automatic movement correction

Using the motion sensor, the operator can place a sensor on the patient that will detect patient movements after co-registration and automatically correct the changes to maintain the same alignment between the US and the second modality dataset.

### 2. Breathing compensation

The motion sensor can also be used to detect the patient's respiratory phases since breathing determines a roto-translation of the liver that can lead to a mismatch of considerable size. A traffic light will indicate the best matching breathing position, while an interpolation algorithm will make the second modality breath synchronously **(Fig. 21)**.

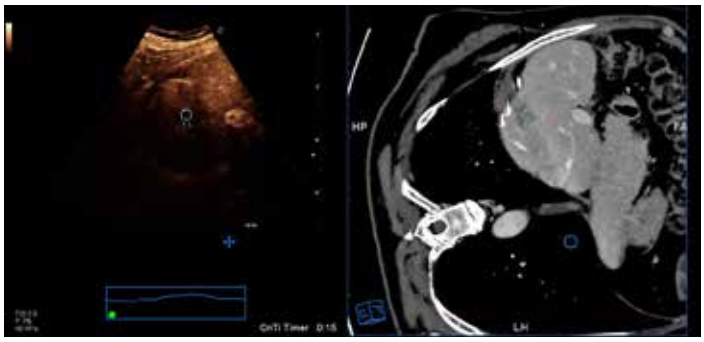


*Fig. 21: Fusion imaging procedure using Breathing synchronization tool to increase the accuracy of the alignment*

### 3. AutomaticRegistration based on hepatic segmentation

The automatic registration algorithm works simultaneously on the US and the second imaging modality volume dataset. It is based on automatically matching the vessels visible in both modalities. Automatic registration with hepatic anatomical markers, usually the vascular tree, was carried out by acquiring a US plan with colour doppler of the hepatic vascular tree, and the automatic vessels detection tool of the MRI/CT dataset.

### 4. AutomaticRegistration with omniTRAX™*

VNav is compatible with CIVCO disposables, and omniTRAX™ is available for MRI and CT acquisition. omniTRAX™ must be used as the second modality of acquisition from the patient. Once the patient arrives for the fusion procedure with the omniTRAX™ in strictly the same position, all the operator needs to do is position the sensor on the omniTRAX™ and confirm the co-registration.

### 5. Needle Tracking

Esaote Needle Tracking technology is additional support for interventional procedures. This feature will enable the virtual path of the needle **(Fig. 22)** to find the best approach and insertion point to reach the target.

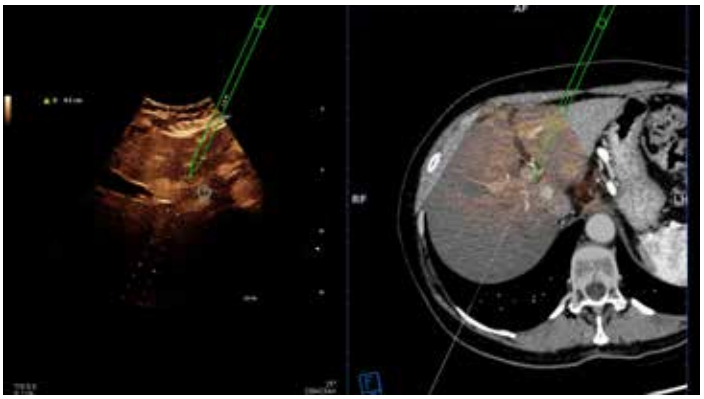


*Fig. 22: Needle Tracking tool to identify the best path to reach the target*

## 6. Planning

VNav offers the option to plan the focal treatment and enable the treated areas according to the chosen therapy.

## Liver Total Approach solution

Furthermore, the Virtual Navigator makes it possible to combine different ultrasound Esaote technologies, such as Colour and Power Doppler, microV, QElaXto 2D, and CnTI™ in real-time during fusion imaging.

Using all the different ultrasound imaging techniques in real-time enables comprehensive imaging and characterisation of the vascularisation of liver lesions[54,55].

*omniTRAX™ is a trademark of CIVCO Medical Solutions

## Liver Total Approach solution - Case report

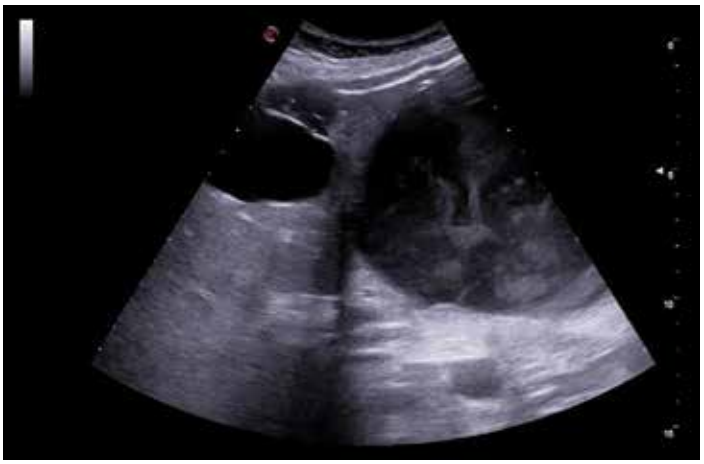


*Fig. 23: Complex liver lesion in grayscale obtained with ultrasound examination*

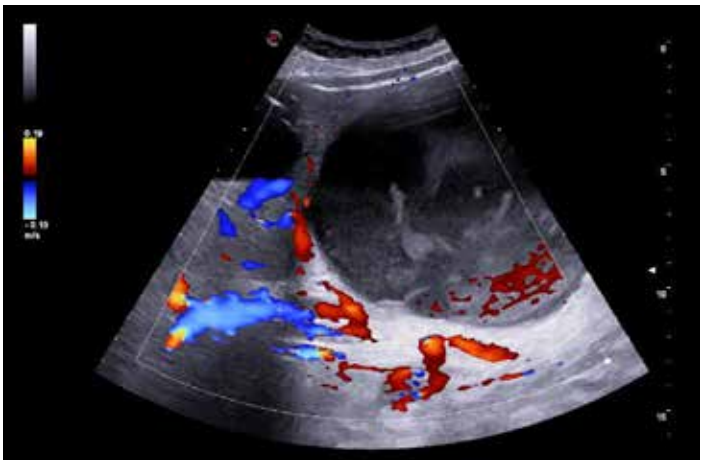


*Fig. 24: No vascularization in color Doppler mode*

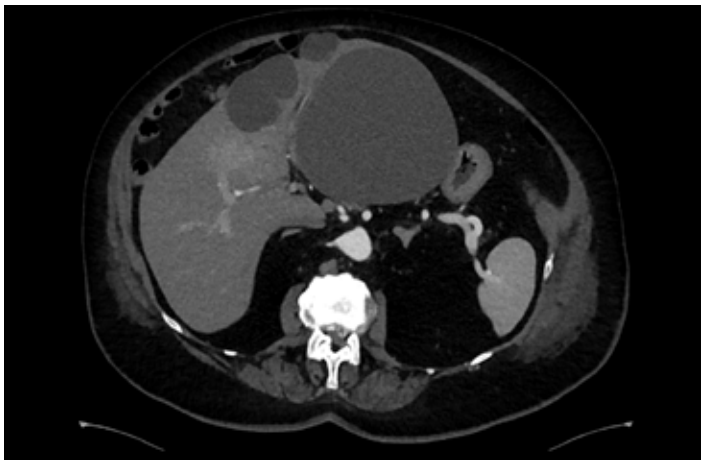


*Fig. 25: Same liver complex lesion detected by CT*

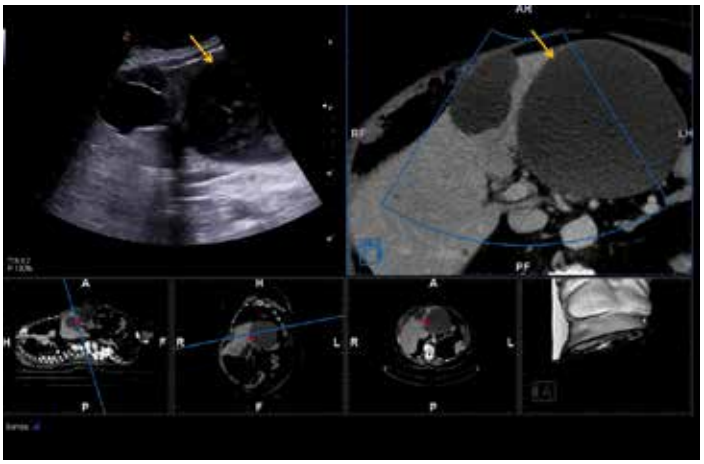


*Fig. 26: Image fusion with B-Mode and CT-data in the side-by-side setting. Patient was referred for ultrasound examination due to increased HE value of the liver cyst in CT. B-Mode sonography of the liver cysts with inhomogeneous multiple septa (yellow arrow). With the help of image fusion, the cyst can be easily detected with multiple septa and thickened walls (yellow arrow) in comparison with MS-CT.*

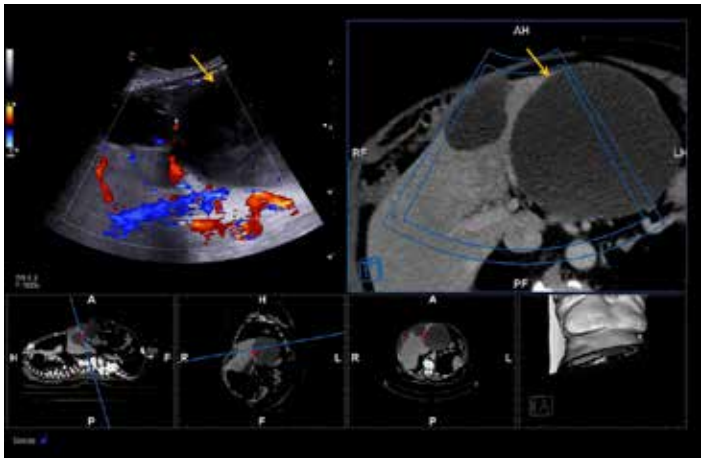


*Fig. 27: Image fusion with color Doppler and CT data in the side-by-side mode. Color Doppler reveals no vascularization of the liver cyst in comparison with CT*

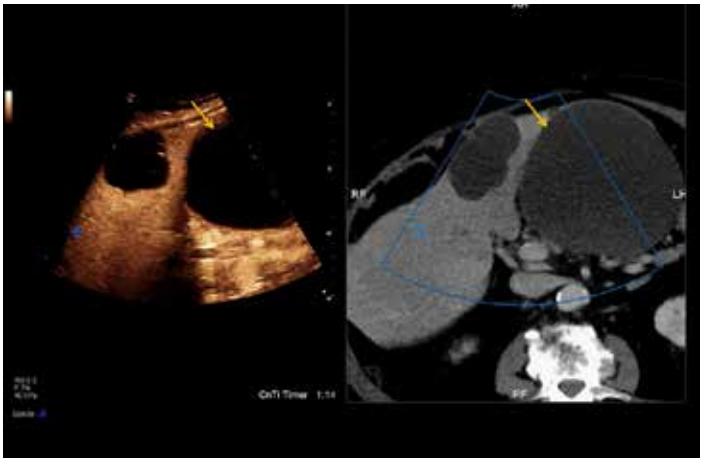


*Fig. 28: CEUS reveals no vascularization of the liver cyst in the side-by-side mode, which is in line with a hemorrhagic liver cyst (yellow arrows)*

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